Improved technique for directly converting skin to neurons

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This is the way things often go in science: One group announces a breakthrough. Yah! Then for the next several years, scientists all over the world replicate and improve on that breakthrough until it's finally believable and widely useful.

To people outside science who read about the initial breakthrough, this may look a lot like scientists twiddling their thumbs, sitting on new therapies. But really, do you want a therapy based on a breakthrough that may or may not be real? Right, neither do I.

A paper from Marius Wernig's lab at Stanford University is a great example of this process. In January, 2010, Wernig's lab had a paper in *Nature* announcing their transformation of mouse skin cells directly into neurons. This was exciting work, bringing with it the possibility of directly converting skin from a person with a neuronal disease into neurons that can be studied in the lab. But that work was in mice, and one thing we know from past research is that mice are most certainly not humans.

About a year and a half later, Wernig replicated his work with human cells in another *Nature* paper, but the transformation was much less efficient than it was with mouse cells (here's our blog entry on that work). It took weeks for the transformation to take place, only 2 to 4 percent of the skin cells transformed into neurons and those neuronal cells were on the wimpy side. It's still exciting work - I mean how cool is it that human skin can be turned into neurons with the addition of just four molecules. But ready for therapeutic prime time? I think not.

Now we've entered the next stage where scientists all over the world incrementally improve upon the original work until it's good enough, fast enough and efficient enough to be broadly useful. One such improvement came from the Stanford University lab of Gerald Crabtree, who published his findings in a *Nature* paper last week.

Crabtree's lab employed two of the four factors that had been effective for Wernig, but supplemented those with a different kind of molecule - called microRNAs. This change dramatically improved how efficiently the skin cells converted to neurons, and produced neurons with much stronger electrical signaling. Another group from Milan published a paper in early July using three different factors to coerce the transformation from skin to neuron. In their case, the neurons were more like those that are lost in Parkinson's disease, known as dopaminergic neurons.

A Stanford press release quotes Crabtree:

> "It's been a long time in coming to this," said Crabtree. "But science often progresses in leaps and starts, and then all of a sudden many scientists come to the same position at the same time. Now these studies have come out, and more will be coming, all of which are going to say that not only can you can make neurons different ways, but also you can make neurons of different types."

At this point it's too soon to know which, if any, of these techniques is going to become most widely used. We can probably expect to see more improvements on these approaches coming out of some labs, while other labs start figuring out how this revolutionary transformation can be used to treat or understand disease. Crabtree's lab, for example, says they are already taking skin cells from people with Down's syndrome and transforming those into neurons in order to understand the disease and look for therapies.

A.A.

Tags: crabtree, Wernig, Stanford University